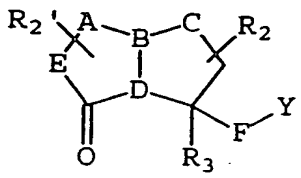
Claims

What is claimed is:

1. A method for inhibiting a protease, comprising administering to an animal in need thereof an effective amount of a compound having the structure:



and pharmaceutically acceptable salts thereof,

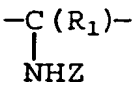
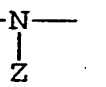
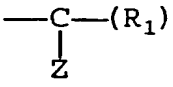
wherein

A is selected from -C(=O)-, $-(CH_2)_{0-4}-$, $-C(=O)(CH_2)_{1-3}-$, $-(CH_2)_{1-2}O-$ and $-(CH_2)_{1-2}S-$;

B is selected from N and CH;

C is selected from -C(=O)-, $-C(=O)(CH_2)_{1-3}-$, $-(CH_2)_{0-3}-$, -O-, -S-, $-O-(CH_2)_{1-2}-$ and $-S(CH_2)_{1-2}-$;

D is selected from N and $C(R_4)$;

E is selected from  ,  and  ;

F is an optional carbonyl moiety;

R_1 and R_4 are independently selected from amino acid side chain moieties and derivatives thereof;

R_2 and R_2' represent one or more ring substituents individually selected from an amino acid side chain moiety and derivatives thereof, or R_2 taken

together with C or Y forms a fused substituted or unsubstituted homocyclic or heterocyclic ring;

R_3 is selected from an amino acid side chain moiety and derivatives thereof, or taken together with C forms a bridging moiety selected from $-(CH_2)_{1-2}-$, -O- and -S-;

Y and Z represent the remainder of the molecule; and

any two adjacent CH groups of the bicyclic ring may form a double bond.

2. The method of claim 1 wherein E is $\begin{array}{l}-C(R_1)-\\ \quad|\\ \quad NHZ\end{array}$.

3. The method of claim 1 wherein E is $\begin{array}{l}-N-\\ \quad|\\ \quad Z\end{array}$.

4. The method of claim 1 wherein E is $\begin{array}{l}-C-(R_1)\\ \quad|\\ \quad Z\end{array}$, with the proviso that Z does not contain an -NH- moiety attached to the carbon atom bearing the R_1 substituent.

5. The method of claim 1 wherein the protease is a serine protease.

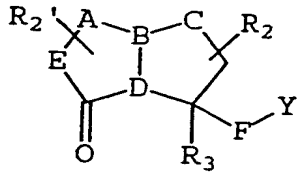
6. The method of claim 5 wherein the serine protease is selected from thrombin, Factor X, Factor IX, Factor VII, Factor XI, urokinase, HCV protease, chymase, tryptase and kallikrein.

7. The method of claim 5 wherein the serine protease is thrombin.

8. The method of claim 5 wherein the serine protease is Factor VII

9. The method of claim 1 wherein the protease is selected from an aspartic, cysteine and metallo protease.

10. A method for inhibiting a kinase, comprising administering to an animal in need thereof an effective amount of a compound having the structure:



and pharmaceutically acceptable salts thereof,

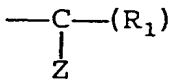
wherein

A is selected from $-C(=O)-$, $-(CH_2)_{0-4}-$, $-C(=O)(CH_2)_{1-3}-$, $-(CH_2)_{1-2}O-$ and $-(CH_2)_{1-2}S-$;

B is selected from N and CH;

C is selected from $-C(=O)-$, $-C(=O)(CH_2)_{1-3}-$, $-(CH_2)_{0-3}-$, $-O-$, $-S-$, $-O-(CH_2)_{1-2}-$ and $-S(CH_2)_{1-2}-$;

D is selected from N and $C(R_4)$;

E is selected from  ,  and  ;

F is an optional carbonyl moiety;

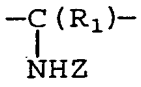
R_1 and R_4 are independently selected from amino acid side chain moieties and derivatives thereof;

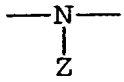
R_2 and R_2' represent one or more ring substituents individually selected from an amino acid side chain moiety and derivatives thereof, or R_2 taken together with C or Y forms a fused substituted or unsubstituted homocyclic or heterocyclic ring;

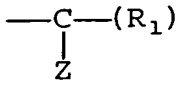
R_3 is selected from an amino acid side chain moiety and derivatives thereof, or taken together with C forms a bridging moiety selected from $-(CH_2)_{1-2}-$, -O- and -S-;

Y and Z represent the remainder of the molecule; and

any two adjacent CH groups of the bicyclic ring may form a double bond.

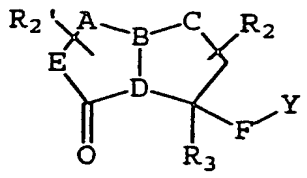
11. The method of claim 10 wherein E is  .

12. The method of claim 10 wherein E is  .

13. The method of claim 10 wherein E is  , with the proviso that Z does not contain an -NH- moiety attached to the carbon atom bearing the R_1 substituent.

14. The method of claims 10 wherein the kinase is a serine/threonine or tyrosine kinase.

15. A method for inhibiting a transcription factor, comprising administering to an animal in need thereof an effective amount of a compound having the structure:



and pharmaceutically acceptable salts thereof,

wherein

A is selected from -C(=O)-, $-(CH_2)_{0-4}-$, $-C(=O)(CH_2)_{1-3}-$, $-(CH_2)_{1-2}O-$ and $-(CH_2)_{1-2}S-$;

B is selected from N and CH;

C is selected from -C(=O)-, $-C(=O)(CH_2)_{1-3}-$, $-(CH_2)_{0-3}-$, -O-, -S-, $-O-(CH_2)_{1-2}-$ and $-S(CH_2)_{1-2}-$;

D is selected from N and $C(R_4)$;

E is selected from $-\underset{\underset{NHZ}{|}}{C}(R_1)-$, $-\underset{\underset{Z}{|}}{N}-$ and $-\underset{\underset{Z}{|}}{C}-(R_1)$;

F is an optional carbonyl moiety;

R_1 and R_4 are independently selected from amino acid side chain moieties and derivatives thereof;

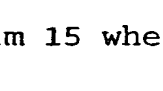
R_2 and R_2' represent one or more ring substituents individually selected from an amino acid side chain moiety and derivatives thereof, or R_2 taken together with C or Y forms a fused substituted or unsubstituted homocyclic or heterocyclic ring;

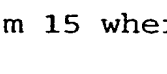
R_3 is selected from an amino acid side chain moiety and derivatives thereof, or taken together with C

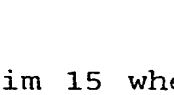
forms a bridging moiety selected from $-(CH_2)_{1-2}-$, -O- and -S-;

Y and Z represent the remainder of the molecule; and

any two adjacent CH groups of the bicyclic ring may form a double bond.

16. The method of claim 15 wherein E is  .

17. The method of claim 15 wherein E is  .

18. The method of claim 15 wherein E is  , with the proviso that Z does not contain an -NH- moiety attached to the carbon atom bearing the R_1 substituent.

19. The method of claim 15 wherein the ability of the transcription factor to bind DNA is controlled by reduction of a cysteine residue by a cellular oxidoreductase.

20. The method of claim 15 wherein the transcription factor is selected from NF-κB, AP-1, Myb, GRE, STAT-1 through -6, NFAT, IRF-1 and MAF.

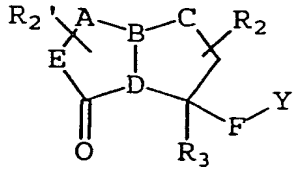
21. The method of claim 15 wherein the transcription factor is NF-κB.

22. The method of claim 15 wherein the transcription factor is AP-1.

23. The method of claim 19 wherein the cellular oxidoreductase is ref-1.

24. The method of claim 15 wherein the warm-blooded animal has been diagnosed with, or is at risk of developing, a condition selected from Crohn's disease, asthma, rheumatoid arthritis, ischemia-reperfusion injury, GVHD, ALS, Alzheimer's disease, allograft rejection, adult T-cell leukemia, cancer and inflammatory bowel disease.

25. A method for inhibiting protein-protein binding interactions, comprising administering to an animal in need thereof an effective amount of a compound having the structure:



and pharmaceutically acceptable salts thereof,

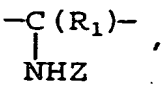
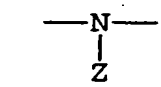
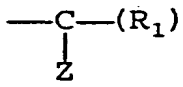
wherein

A is selected from -C(=O)-, $-(CH_2)_{0-4}-$, $-C(=O)(CH_2)_{1-3}-$, $-(CH_2)_{1-2}O-$ and $-(CH_2)_{1-2}S-$;

B is selected from N and CH;

C is selected from -C(=O)-, $-C(=O)(CH_2)_{1-3}-$, $-(CH_2)_{0-3}-$, -O-, -S-, $-O-(CH_2)_{1-2}-$ and $-S(CH_2)_{1-2}-$;

D is selected from N and $C(R_4)$;

E is selected from  ,  and  ;

F is an optional carbonyl moiety;

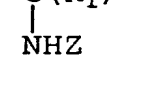
R_1 and R_4 are independently selected from amino acid side chain moieties and derivatives thereof;

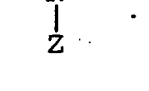
R_2 and R_2' represent one or more ring substituents individually selected from an amino acid side chain moiety and derivatives thereof, or R_2 taken together with C or Y forms a fused substituted or unsubstituted homocyclic or heterocyclic ring;

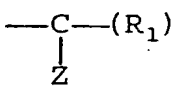
R_3 is selected from an amino acid side chain moiety and derivatives thereof, or taken together with C forms a bridging moiety selected from $-(CH_2)_{1-2}-$, -O- and -S-;

Y and Z represent the remainder of the molecule; and

any two adjacent CH groups of the bicyclic ring may form a double bond.

26. The method of claim 25 wherein E is  .

27. The method of claim 25 wherein E is  .

28. The method of claim 25 wherein E is  , with the proviso that Z does not contain an -NH- moiety attached to the carbon atom bearing the R_1 substituent.

29. The method of claim 25 wherein the protein-protein binding interaction is between the SH2 domain or the PDZ domain and another protein.